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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,303	02/26/2004	Kelly Reed Clark	28335/40012	8089

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EXAMINER	
BURKHART, MICHAEL D	
ART UNIT	PAPER NUMBER
1633	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/20/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/789,303	CLARK ET AL.	
	Examiner	Art Unit	
	Michael D. Burkhart	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,18,19 and 21-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *19* is/are allowed.

6)☒ Claim(s) *1-14,18 and 21-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt and entry of the amendment dated 10/6/2006 is acknowledged. After entry of the amendment, claims 1-14, 18, 19 and 21-38 are pending and under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **These rejections are maintained for reasons made of record in the previous Office Actions and for reasons set forth below.**

Claim 1 recites, in the last two lines, a rAAV-producing cell that "overexpresses AAV Rep 52 and Rep 40 proteins." It is unclear what the point of reference is for the overexpression of the Rep 52/40 proteins: overexpressed compared to what? For example, is the overexpression compared to Rep 52/40 expression mediated by the wild type AAV promoter, or to expression mediated by a constitutive, heterologous promoter such as a CMV promoter? Furthermore, cells not infected with AAV do not express Rep 52/40 proteins, thus, any cell that expresses Rep 52/40, at any detectable level, might be considered to "overexpress" Rep 52/40 with respect to an uninfected cell line. It cannot be determined from the claims which, if any, if the above situations would constitute infringement of the claimed subject mater. For this reason, the metes and bounds of the subject mater are unclear. This rejection affects all dependent claims.

Claim 9 recites a rAd "derived from" simian Ad SV-20. It cannot be determined how close to the original or wild-type SV-20 the derivative rAd must be in order to infringe the claimed subject matter. Therefore, the metes and bounds of the claimed subject matter are unclear.

Response to Arguments

Applicant's arguments filed 10/6/2006 have been fully considered but they are not persuasive. Regarding claim 1, applicants essentially assert that: 1) one of skill in the art would understand that the term "overexpress" means relative to expression driven by the native p19 promoter; 2) the Examples in the specification describe "overexpression" relative to that driven by the p19 promoter. Neither of these arguments is convincing because limitations found in the specification, such as using the term "overexpress" to be relative to the p19 promoter, are not to be read into the claims. See MPEP §2111.01 (II), which states:

> "Though understanding the claim language may be aided by explanations contained in the written description, it is important not to import into a claim limitations that are not part of the claim. For example, a particular embodiment appearing in the written description may not be read into a claim when the claim language is broader than the embodiment."

In this situation, the limitation "overexpresses AAV Rep 52 and Rep 40 proteins" is broader than the example(s) in the specification relied upon by applicants. The remainder of the specification provides no further guidance on the interpretation of "overexspression", which may be interpreted several ways (see above). Thus, the claimed subject matter is unclear.

Regarding claim 9, applicants essentially assert that: 1) the term "derived from" indicates the claimed adenovirus vectors were constructed using simian adenovirus SV-20; and, 2) methods to modify adenoviruses in order to construct adenoviral vectors are well known in the

art. Regarding 1), it remains unclear how close to the original SV-20 the claimed derivative(s) might be. For example, how much of the SV-20 genome could be deleted, or replaced with foreign sequences, and the rAd still be considered "derived" from SV-20? Regarding 2), methods to modify wild-type adenoviruses are indeed well-known in the art, but this issue was not in contention and this argument appears more suited as a response to a U.S.C. 112 1st¶ enablement rejection. One of skill in the art could indeed modify wild-type adenoviruses using established methods. However, what is unclear is the extent of such modification required to read on the claimed subject matter.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-14, 21-29, and 31-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of producing rAAV or rAAV-producing cells by transfection or transformation of cells with nucleic acids encoding the desired proteins, does not reasonably provide enablement for such methods by "providing" AAV helper functions (as recited in claim 3) or introducing proteins into a cell (claim 10). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. **This rejection is maintained for reasons made of record in the previous Office Action and for reasons set forth below.**

Response to Arguments

Applicant's arguments filed 10/6/2006 have been fully considered but they are not persuasive. Applicants essentially assert that: 1) AAV helper functions were well known in the art at the time of filing; 2) numerous references detailing how to use helper functions to generate AAV-generating cells are found in the specification, as are exemplified embodiments of the instant methods.

Regarding 1), this is not in dispute, hence the scope of enablement rejection. Regarding 1) and 2), all of the references, and the instant specification, teach providing nucleic acids, not proteins, to cells in order to generate AAV-producing cells. Delivering such nucleic acids is within the scope embraced by the instant claims, and is considered enabled. Furthermore, a reading of the references only serves to bolster the scope of enablement rejection because it underscores that methods of delivering proteins into cells in order to generate AAV-producing cells (or delivery of proteins in general) were unknown in the art at the time of filing, and therefore would require undue experimentation in order to establish such methods.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 10-13, 18, 21, 23, 24, 30, 32 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Natsoulis et al (U.S. Patent 6,027,931, 2000).

Claims 1-2, 10-13, 18, 21, 23, 24, 30, 32 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Xiao et al (J. Virol., 1998).

These rejections are maintained for reasons made of record in the previous Office Actions and for reasons set forth below.

Response to Arguments

Applicant's arguments filed 10/6/2006 have been fully considered but they are not persuasive. Because the arguments relating to Natsoulis et al and Xiao et al are essentially the same, they are addressed together. Applicants essentially assert that: 1) the AAV-producing cell of claim 1 has been amended to recite that the expression level of Rep 78/68 has not been genetically down-regulated, a limitation not taught by Natsoulis et al nor Xiao et al; and, 2) claim 3 requires that the expression cassette by introduced subsequently to cells already comprising an AAV genome and rep-cap proteins.

Regarding 1), the cells of claim 1 require expression of Rep 78/68 proteins "at about the level of expression of the proteins when under control of the AAV p5 promoter." As such, the claims embrace a wide range of expression levels of these proteins (explained in the previous Office Action dated 4/4/2006). The limitation that these expression levels are not achieved by genetic down-regulation is a product-by-process limitation. Such claims are not limited by the process steps, but rather by the product implied by the steps. See MPEP §2113:

> "If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process."

In this case, the prior art cells still express levels of Rep 78/68 considered to be "about" the levels expressed by the p5 promoter for reasons made of record, and thus anticipate the instant claims.

Regarding 2), it was explained in the Office Action dated 7/29/2005 (page 6, first full ¶) that Natsoulis et al taught the addition of Rep/Cap expression constructs (which express Rep 52/40) sequentially to cells comprising an AAV vector, which also comprises rep-cap coding sequences.

Thus it is considered that Natsoulis et al and Xiao et al anticipate the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 22, 26, 28, 29, 31, 35, 37, and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Natsoulis et al (6,027,931) as applied to claims 1-3, 10-13, 18, 21, 23, 24, 30, 32 and 33 above, and further in view of Hardy (U.S. Patent 6,429,001, 2002).

Claims 25 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Natsoulis et al (6,027,931) as applied to claims 1-3, 10-13, 18, 21, 23, 24, 30, 32 and 33 above, and further in view of Murphy (U.S. Patent 6,635,476, 2003, effective filing date of 10/15/1999).

Claims 27-29 and 36-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Natsoulis et al and Hardy as applied to claims 1-3, 10-13, 18, 21-24, 26, 28-33, 35, 37, and 38 above, and further in view of Potash et al (U.S. Patent 5,911,998, 1999).

These rejections are maintained for reasons made of record in the previous Office Actions and for reasons set forth below.

Response to Arguments

Applicant's arguments filed 10/6/2006 have been fully considered but they are not persuasive. Because the arguments relating to the above 35 USC §103 rejections are essentially the same, they are addressed together. Applicants essentially assert that Natsoulis et al does not teach all the instant claim limitations, and the other documents cited above do not remedy the deficiency of Natsoulis et al. This is not persuasive because for reasons set forth above, Natsoulis et al is still considered anticipatory for claims 1-3, 10-13, 18, 21, 23, 24, 30, 32 and 33. Therefore, it is considered the above claims are rendered obvious as set forth above and as set forth in the previous Office Actions.

Conclusion

Claim 19 is allowed. The prior art of record does not teach or suggest the use of SV-20 to infect (and complement) rAAV-producing cells.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael D. Burkhart whose telephone number is (571) 272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michael D. Burkhart

Examiner

Art Unit 1633

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER